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Measurement of Sublingual Blood Velocity as a Tool for Monitoring Sepsis

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Abstract

Measurements of sublingual blood velocity and blood flow were performed at normal body temperature and after both hot and cold stimulation. Laser speckle measurements of blood velocity were compared with measurements of blood flow obtained with a commercial laser Doppler flowmeter. Sublingual blood velocity increased in all subjects in response to both hot and cold stimulation as compared with that at normal temperature.

I. Introduction

In healthy subjects, the sublingual blood circulation is a dense network of vessels. During organ injury, significant changes in microvascular hemodynamics occur. Currently, there exist no noninvasive monitoring techniques that provide realtime and quantitative assessment of sublingual microcirculation. The orthogonal polarization microscopy (OPM) method has been used to identify the nature of microcirculatory dysfunction in sepsis, but the data are not quantitative or reproducible [1]. Plethysmography has been used to measure qualitative fluctuations in the blood volume. Taking advantage of the optical coherent effect, two laser-based techniques, laser speckle imaging (LSI) and laser Doppler imaging (LDI), have been applied to measure the movement of red blood cells (RBCs). The LDI is used to measure the flux of the RBCs. It is usually employed for point measurements. It demands a scanning mechanism for 2D image mapping. The LSI measures the speckle contrast which is then used to obtain blood velocity information.

II. Laser Speckle Imaging

Laser speckle was initially viewed as a noise term until its recent application as a means of measuring velocities. Temporal variations of the speckle contrast at every point on the image are extracted from the acquired laser speckle pattern. Spatial distribution of the speckle image is obtained by computing the average intensity $\langle I(x, y) \rangle$ and the speckle contrast $d(x, y)$ over a pre-defined neighborhood of a point (x, y) . The speckle contrast is defined by:

$$d(x, y) = \frac{\sigma(x, y)}{\langle I(x, y) \rangle} \quad (1)$$

where $\sigma(x, y)$ is the standard deviation of intensity over the pixel neighborhood. The speckle contrast values are related to blood flow velocity distribution [2]. Flow velocities are obtained

from spatial statistics analysis using multiple scattering analysis of two or more images of the same scene at different exposures.

III. Experimental Methods

Sublingual blood velocity data at different sublingual temperatures were collected from healthy subjects (n=20) using the LSI technique. For comparison purposes, the sublingual area was also measured on two healthy subjects using the LDI technique.

A. LSI Measurement

Figure 1 shows a block diagram of the LSI system. A He-Ne laser (1.5 mW, 632.8 nm) was used as the light source to provide a stable and well-defined Gaussian beam. The laser radiation was delivered to the sublingual area via an optical fiber. A high-performance, monochrome, CCD camera (DVC 4000M-00-GE) was used to capture the LSI images. It utilizes an on-chip electronic shutter and circuitry for gain, exposure, offset, and frame rate adjustments. The CCD has a pixel size of $7.4 \mu\text{m} \times 7.4 \mu\text{m}$ and a peak quantum efficiency of more than 55%. A zoom lens assembly was attached to the camera to collect the scattered radiation to fill the CCD's active area of 2048×2048 pixels. The speckle size was set to match that of the pixel size by using an adjustable field stop on the lens.

Accuracy of the velocity retrieval from speckle images improves if one uses short exposure for high velocity measurements and long exposure for low velocity measurements. Speckle contrast increases with increasing exposure. Two exposures, 2 ms and 4 ms, were used for sublingual blood velocity measurements.

B. LDI Measurement

The LDI used is a moorLDI2 (Moor Instruments, moor.co.uk). After selecting the scan region of interest (ROI), each sublingual measurement session took about 60 s. The LDI measurement results are in the form of a flux image.

C. Study Protocol

The study consisted of measuring the sublingual blood velocity of 20 apparently healthy subjects (11 men; range 22–48 years; mean 30 ± 4 years). The study protocol, informed consent, and case report form were approved by the Institutional Review Board (IRB) of Riverside Regional Medical Center (Newport News, VA). Before the measurements, subjects were instructed not to consume caffeine, alcohol, food, or smoke at least three hours prior to data collection. After obtaining the signed informed consent, subjects were requested to complete the subject characteristic portion (age, gender, and racial information) of the case report form. The subject's body temperature, blood pressure, and heart rate were measured by the study researchers and recorded. Measurement sessions were then conducted as follows:

1. A pulse oximeter was attached to the subject's right index finger. This signal is used to trigger data acquisition.
2. The subject placed his/her chin on a chin rest to minimize motion effect.
3. The subject then opened his/her mouth, raising the tongue to expose the sublingual area.
4. The instrument was aimed at the sublingual area and manually focused. A sequence of images were acquired to collect baseline temperature information.
5. The subject was then asked to repeatedly swish his/her mouth with warm water ($T_{\text{av}}=55.4^\circ\text{C}$). Steps 2 through 4 were then repeated.

6. The subject was then asked to repeatedly swish his/her mouth with cold water ($T_{av}=3.7^{\circ}\text{C}$). Steps 2 through 4 were then repeated.
7. The measurements may be repeated and image data collected by a second operator to obtain reproducibility information.

Sublingual blood flow of two apparently healthy subjects (a 22-year-old Caucasian female and a 24-year-old Caucasian male) was also measured using the LDI. Images were collected at normal, warm, and cold temperatures. Each scan of the sublingual area took about 60 s, which made it difficult to accurately record the temperature changes during the measurement session.

D. Data Analysis

The value of the speckle contrast at every image pixel was computed using (1). The variance, σ^2 , of the spatial intensity is equivalent to the time average of the autocovariance, $C_v(\tau)$, of the intensity fluctuations,

$$\sigma^2(T) = \frac{1}{T} \int_0^T C_v(\tau) d\tau \quad (2)$$

where T is the integration time.

For stationary processes, the single-scattering approximation of $C_v(\tau)$ can be written as a decaying exponential with a correlation time τ_c . Equating $\sigma(x,y)$ in (1) with $\sigma(T)$ in (2), a characteristic velocity can be obtained,

$$V_c = \frac{\lambda}{(2\pi\tau_c)} \quad (3)$$

Figure 2 shows the relationship between speckle contrast and characteristic velocity.

Multiple scattering from flowing RBCs and stationary tissue complicates the procedure for retrieving blood velocities from intensity fluctuations. Evolution of the phase difference of the scattered light can be treated as a series of scattering events. One applies the autocorrelation function, $C_I(\tau)$, of the speckle contrast intensity to retrieve velocity,

$$C_I(\tau) = 1 + \beta (\exp(2m[I_i(\tau) - 1]) - \exp(-2m)) \quad (4)$$

where β is the optical coherence of the signal at the viewing position, m is the average number of collisions the photon undergoes with a moving particle, and $I_i(\tau)$ is an intermediate scattering function containing the velocity dependence of the scattering by the RBCs. Multiple scattering effects are incorporated by calculating d , obtaining σ from (2), and evaluating $C_I(\tau)$. Both β and m are obtained from examining the scattering process, and $I_i(\tau)$ can be evaluated as a function of blood velocity distribution.

IV. Results

Figure 3 shows a typical image of the illuminated sublingual area. A typical set of three velocity mapping images taken at different temperatures, 25.9°C (top), 36.4°C (middle), and 41.4°C (bottom), is shown in false color in Fig. 4. The images shown are from Subject #12 (a 24-year-

old Caucasian male). Sublingual blood velocities ranged from 0.15 mm/s to 0.7 mm/s for all three temperatures. The velocity distributions for both warm and cold temperatures shift to higher values from that of the normal temperature. Fig. 5 shows a typical image of the sublingual scan area and the resulting flux image taken with the moor instrument. Values (in arbitrary unit) of the mean and standard deviation of the measured sublingual blood flow at cold, normal, and hot temperatures are 784 ± 384 , 569 ± 300 , and 660 ± 63 , respectively.

V. Discussions

The increase of sublingual blood velocity at both hot and cold temperatures from that at normal temperature is observed at all 20 subjects. This effect is also observed in the LDI measurements of the two subjects. Due to the long scanning time (60 s) for the LDI measurements, the effect of motion artifacts can be clearly seen in Fig. 5.

Using the laser Doppler velocimetry, Heckmann et al. [3] and Heckmann et al. [4] investigated the effect of cold stimulation on the microcirculatory responses in the oral cavity of a group of healthy control subjects only, and the controls and the burning mouth syndrome (BMS) patients, respectively. They found that in both control and BMS groups, the mucosa blood flow increases in response to the cold stimulation and this increase tends to return to that at normal temperature with no significant changes in heart rate or blood pressure.

It may be explained that the autoregulation is much more pronounced in the sublingual area than that in the extremities, such as the hand. The blood flow data of the hand measured with the moor LDI show a slower flow at cold temperature (152 ± 92 a.u.) and a faster flow at warm temperature (650 ± 433 a.u.) than that at normal temperature (355 ± 203 a.u.). The same trend was also observed in the hand measurements using the LSI [5]. Heckmann et al. [3] attribute the behavior of oral mucosa blood flow to the complex innervation from cranial parasympathetic, superior cervical sympathetic, and trigeminal nerves, indicating a specific and unique regulatory mechanism for the area.

VI. Conclusions

Sublingual blood flow velocity values were obtained on healthy subjects at varying sublingual temperatures using both LSI and LDI techniques. The measurement results from both methods agree for all subjects. Additionally, the results agree with those observed by Heckmann et al. [3] and Heckmann et al. [4]. Future research involves the application of the LSI technique on ICU patients to further investigate the potential of the technique for monitoring early signs of sepsis.

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Fig. 1.
Block diagram of the LSI system.

Fig. 2.
Relationship between speckle contrast and LSI velocity at five different exposures.

Fig. 3.
An unprocessed image of the sublingual area.

Fig. 4. Sublingual blood velocity mappings at cold (top), normal (middle), and hot (bottom) temperatures.

Fig. 5.
LDI images, left-unprocessed; right-flux in false color.